

vol. 3, no. 3, 1 Jan. 2013 (2014-01-01), XP055406815, discloses the potential effectiveness of canine cells or its conditioned media in the treatment of wounds in different species such as in diabetic rats, such wounds are made by making a full thickness excision in the skin of the rat. On the contrary, skin inflammation causing atopic dermatitis rash is considered a type of allergic response. Therefore, the treatment of wounds generated in Mohd Matin Ansari et al and the treatment of atopic dermatitis are completely unrelated.

**[0014]** Finally, WO2017144552 is explicitly directed to compositions that mandatorily comprise dimethyl sulfoxide (DMSO), in fact DMSO is an essential feature in WO2017144552 since it enhances the treatment of the diseases detailed therein. However, WO2017144552 is not directed to the xenogeneic treatment of human atopic dermatitis or psoriasis, particularly in the context of a DMSO free composition, by using conditioned cell culture mediums obtained or obtainable by a process which comprises culturing a population of mesenchymal stromal cells (MSCs), wherein at least 50% of said population by number of cells are MSCs obtained from a mammal pertaining to the genus *canis*.

**[0015]** Therefore, the present invention is, as far as we know, the first to provide a composition comprising a conditioned cell culture medium obtained or obtainable by a process which comprises culturing a population of mesenchymal stromal cells (MSCs), wherein at least 50% of said population by number of cells are MSCs obtained from a mammal pertaining to the genus *canis*, for use in the xenogeneic treatment of human atopic dermatitis.

#### BRIEF DESCRIPTION OF THE INVENTION

**[0016]** According to the invention, instead of using stem cells, injured or lost tissues may be regenerated or repaired through enhancement of endogenous tissue repair by applying secretions from MSCs instead of, or in addition to, MSCs themselves. Specifically, we provide for the use of conditioned media in which the MSCs derived from a mammal pertaining to the genus *canis* are cultured in order to obtain such conditioned media suitable for the treatment of skin inflammatory disorders such as psoriasis or atopic dermatitis.

**[0017]** In particular, in table II (see description) we show a qualitative and quantitative comparison of the polypeptides secreted by MSCs from a mammal pertaining to the genus *canis* and those secreted from other mammals such as MSCs from cats or humans. In addition, the examples disclosed in the present specification clearly show a therapeutic effect linked to the use of the conditioned media obtained from culturing MSCs derived from a mammal pertaining to the genus *canis*, in particular a therapeutic effect linked to the treatment of atopic dermatitis or psoriasis.

**[0018]** With this approach, the present confounding issues associated with cell based therapy i.e. immune compatibility, tumorigenicity, xenozootic infections, costs, and waiting time if autologous cell preparations are used will be eliminated. Such an approach could potentially provide for the development of "off-the-shelf" MSC-based therapeutics at affordable costs and with better quality control and consistency.

**[0019]** The practice of the present invention will employ, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant

DNA and immunology, which are within the capabilities of a person of ordinary skill in the art. Such techniques are explained in the literature. See, for example, J. Sambrook, E. F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Second Edition, Books 1-3, Cold Spring Harbor Laboratory Press; Ausubel, F. M. et al. (1995 and periodic supplements; *Current Protocols in Molecular Biology*, ch. 9, 13, and 16, John Wiley & Sons, New York, N. Y.); B. Roe, J. Crabtree, and A. Kahn, 1996, *DNA Isolation and Sequencing: Essential Techniques*, John Wiley & Sons; J. M. Polak and James O'D. McGee, 1990, *Oligonucleotide Synthesis: A Practical Approach*, Irl Press; D. M. J. Lilley and J. E. Dahlberg, 1992, *Methods of Enzymology: DNA Structure Part A: Synthesis and Physical Analysis of DNA Methods in Enzymology*, Academic Press; *Using Antibodies: A Laboratory Manual: Portable Protocol NO. 1* by Edward Harlow, David Lane, Ed Harlow (1999, Cold Spring Harbor Laboratory Press, ISBN 0-87969-544-7); *Antibodies: A Laboratory Manual* by Ed Harlow (Editor), David Lane (Editor) (1988, Cold Spring Harbor Laboratory Press, ISBN 0-87969-314-2), 1855; and *Lab Ref: A Handbook of Recipes, Reagents, and Other Reference Tools for Use at the Bench*, Edited Jane Roskams and Linda Rodgers, 2002, Cold Spring Harbor Laboratory, ISBN 0-87969-630-3. Each of these general texts is herein incorporated by reference.

**[0020]** Thus a first aspect of the invention refers to a composition comprising a conditioned cell culture medium obtained or obtainable by a process which comprises culturing a population of mesenchymal stromal cells (MSCs), in which at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99%, of said population by number of cells are MSCs obtained from a mammal pertaining to the genus *canis* or immortalized mesenchymal stromal cells obtained therefrom, in a nutrient rich liquid prepared for cell culture, preferably a basal media, such as DMEM, MEM, RPMI, or HAM'S with or without supplements such as serum containing media, serum free media, protein free media and chemically defined media; and collecting the conditioned cell culture medium,

wherein preferably the nutrient rich liquid is an animal and human serum-free media designed to grow MSCs, and wherein preferably said composition does not comprise dimethyl sulfoxide (DMSO), for use in therapy.

**[0021]** It is preferably noted, that preferably the composition of the first aspect of the invention as a whole does not comprise human and animal serum components.

**[0022]** In a preferred embodiment of the first aspect of the invention or of any of its preferred embodiments, the MSCs are obtained from a mammal pertaining to the dog species.

**[0023]** In another preferred embodiment of the first aspect of the invention or of any of its preferred embodiments, the mesenchymal stromal cells are umbilical-cord derived stromal cells, adipose tissue-derived stromal cells, expanded mesenchymal stromal cells, expanded adipose tissue-derived stromal cells, bone-marrow derived stromal cells, expanded bone-marrow derived stromal cells or immortalized mesenchymal stromal cells obtained from any of the afore mentioned sources.